protein that mediates secretion, a kinase, a G-protein, a cell surface receptor, a GTPase activating protein, a guanine nucleotide exchange factor, a phosphatase, a protease, a phosphodiesterase, a bacterial protein toxin, an importin, an RNA-binding protein, an SCF complex component, an adherin, or a protein encoded within a biosynthetic cluster. In certain other embodiments of the fourth aspect, the variant regulator protein is selected to have more activity in a heterologous cell and/or more activity in a homologous cell. In certain embodiments, the variant regulator protein is selected to have more activity in a heterologous cell and/or more activity in a homologous cell and to cause more secondary metabolite to be produced in a homologous cell and/or a heterologous cell when compared to the cognate, wild-type regulator protein. In a particularly preferred embodiment, the variant regulator protein is a lovE variant regulator protein.

In a fifth aspect, the invention provides an isolated variant regulator protein of secondary metabolite production having increased activity compared to a cognate, wild-type protein, the variant regulator protein made by the process comprising: (a) selecting a nucleic acid comprising a polynucleotide encoding a protein regulator of secondary metabolite production; (b) mutating the nucleic acid to create a plurality of nucleic acid molecules encoding variant regulator proteins of secondary metabolite production; (c) selecting a variant regulator protein with more activity than the cognate, wild-type protein; and (d) recovering the selected variant regulator protein.

In certain embodiments of the fifth aspect, the secondary metabolite is a fungal secondary metabolite. In certain embodiments of the fifth aspect, the protein regulator of secondary metabolite production is a transcription factor. In certain embodiments of the fifth aspect, the protein regulator of secondary metabolite

production is a transmembrane transporter, a protein that mediates secretion, a kinase, a G-protein, a cell surface receptor, a GTPase activating protein, a guanine nucleotide exchange factor, a phosphatase, a protease, a phosphodiesterase, a bacterial protein toxin, an importin, an RNA-binding protein, an SCF complex component, an adherin, or a protein encoded within a biosynthetic cluster. .In certain embodiments of the fifth aspect, the variant regulator protein has more activity in a heterologous and/or a homologous cell than the cognate, wild-type protein. In certain embodiments of the fourth aspect, the variant regulator protein increases production of a secondary metabolite in a heterologous cell and/or a homologous cell when compared to the cognate, wild-type protein. In a particularly preferred embodiment, the variant regulator protein is a lovE variant regulator protein.

In a sixth aspect, the invention provides a fungus having improved lovastatin production made by the process of transforming a fungal cell with a nucleic acid molecule encoding a lovE variant protein of the first aspect of the invention. In an embodiment thereof, the nucleic acid molecule is selected from a nucleic acid molecule of the second aspect of the invention.

In a seventh aspect, the invention provides an improved process for making lovastatin comprising transforming a fungal cell with a nucleic acid molecule encoding a variant of the lovE protein of the first aspect of the invention. In an embodiment thereof, the fungal cell is transformed with a nucleic acid molecule of the second aspect of the invention.

In a eighth aspect, the invention provides a nucleic acid molecule encoding a lovE protein defined by SEQ ID NO:91. In an embodiment thereof, the invention provides an isolated *lovE* nucleic acid molecule defined by SEQ ID NO:92.

BRIEF DESCRIPTION OF THE DRAWINGS

Figure 1 is a photographic representation of cells growing on media with and without G418 selection demonstrating *lovF*p-*HIS3*p-Neo activation in *S. cerevisiae*. Controls include MB968 (vector only), MB2478 (lowly expressed wild-type *lovE*), and MB1644 (highly expressed wild-type *lovE*). All *lovE* variants are expressed in an MB968 vector backbone similar to MB2478.

Figure 2A is a graphic representation of *lovF*p-*CYC1*p-*lacZ* expression in *S. cerevisiae* strains expressing lovE variant proteins from the clones *lovE* 1-10.

Figure 2B is a graphic representation of *lovF*p-*CYC1*p-*lacZ* expression in *S. cerevisiae* strains expressing lovE variant proteins from the clones *lovE* 1-10 from a separate transformation than that of Figure 2A.

Figure 3 is a graphic presentation of *lovF*p-*CYC1*p-lacZ expression in *S. cerevisiae* strains expressing lovE variant proteins from clones *lovE* 16-41.

Figure 4 is a graphic presentation of *lovF*p-lacZ expression in *S. cerevisiae* strains expressing *lovE* variant proteins from clones *lovE* 1-10.

Figure 5 is a graphic presentation of *lovF*p-lacZ expression in *S. cerevisiae* strains expressing lovE variant proteins from clones *lovE* 16, 20, 21, 30-34, and 36-41.

Figure 6 is a graphic presentation of lovastatin culture concentration, as measured by enzyme inhibition assay, from broths of *A. terreus* cultures expressing *lovE* variant proteins 1-10 in.

Figure 7A is a graphic depiction of lovastatin culture concentration, as measured by HPLC analysis, from